

In the Claims:

Please amend claims 1, 2, 5, and 6. Please add new claims 91-94. The claims are as follows:

1. (Currently amended) An oxidized heparin fraction having a molecular weight of from about 2,000 to about 4,000 daltons,

wherein the oxidized heparin fraction is super-sulfated such that the oxidized heparin fraction comprises an anticoagulant reduction characteristic and an angiogenesis inhibition characteristic;

wherein the super-sulfated oxidized heparin fraction has a chemical structure of a first oxidized heparin fraction after the first oxidized heparin fraction has been O-sulfated by sulfate substitution at oxygen bonds at vertexes of repeating units of the first oxidized heparin fraction;

wherein the super-sulfated oxidized heparin fraction comprises a sulfate to carboxylate ratio sufficiently high to fully inhibit angiogenesis.

~~wherein the anticoagulant reduction characteristic comprises a first anticoagulant reduction characteristic, a second anticoagulant reduction characteristic, or a combination thereof;~~

~~— wherein the first anticoagulant reduction characteristic is that the oxidized heparin fraction reduces a mean percent inhibition of platelet clot strength by factor of at least about 8 relative a mean percent inhibition of platelet clot strength of unfractionated heparin under a condition of the concentration of the oxidized heparin fraction in human blood being equal to the concentration of the unfractionated heparin in human blood;~~

—wherein the second anticoagulant reduction characteristic is that the oxidized heparin fraction reduces a prolongation of clotting time of human blood by at least 75% relative to a prolongation of clotting time of human blood by unfractionated heparin under a condition of the concentration of the oxidized heparin fraction in human blood being equal to the concentration of the unfractionated heparin in human blood, subject to the clotting time being a prothrombin time (PT) or an activated partial thromboplastin time (APTT); and

wherein the angiogenesis inhibition characteristic is that the oxidized heparin fraction in an endothelial cell (EC) growth medium cancels an effect of recombinant human fibroblast growth factor (FGF2) on EC tube formation in the EC growth medium under a condition of the concentration of FGF2 in the EC growth medium being sufficient to increase a length or area of the EC tube formation by a factor of at least about 2 if the oxidized heparin fraction is not in the EC growth medium.

2. (Currently amended) The oxidized heparin fraction of claim [[1]] 91, wherein the anticoagulant reduction characteristic comprises the first anticoagulant reduction characteristic.

3-4. (Canceled)

5. (Currently amended) The oxidized heparin fraction of claim [[1]] 91, wherein the anticoagulant reduction characteristic comprises the second anticoagulant reduction characteristic.

6. (Currently amended) The oxidized heparin fraction of claim [[1]] 91, wherein the anticoagulant reduction characteristic comprises the first anticoagulant reduction characteristic and the second anticoagulant reduction characteristic.

7-42. (Canceled)

43. (Previously presented) A composition comprising from about 60% to about 100% of the oxidized heparin fraction of claim 1, and from about 0% to about 40% of heparin, low molecular weight heparin, chondroitin sulfates, dermatan sulfates, heparan sulfates, heparin derivatives, or combinations thereof.

44-48. (Canceled)

49. (Previously presented) The composition of claim 43, further comprising a non-heparin anticoagulant.

50. (Previously presented) The composition of claim 49, wherein the non-heparin anticoagulant is selected from the group consisting of anti-Xa compounds, anti-IIa compounds, anti-tissue factor compounds, anti-VIIa compounds, and combinations thereof.

51. (Previously presented) The composition of claim 43, further comprising a non-heparin angiogenic inhibitor.

52. (Previously presented) The composition of claim 51, wherein the non-heparin angiogenic inhibitor is selected from the group consisting of integrin inhibitory compounds, angiostatin, endostatin, fibroblast growth factor inhibitors, fibroblast growth factor receptor inhibitors, vascular endothelial growth factor inhibitors, thrombospondin, platelet factor 4, interferon, interleukin 12, thalidomide, and combinations thereof.

53. (Previously presented) The composition of claim 43, further comprising a cytotoxic or chemotherapeutic agent.

54. (Previously presented) The composition of claim 53, wherein the cytotoxic or chemotherapeutic agent is selected from the group consisting of nitrogen mustard, aziridine thiotepa, alkyl sulfonate, nitrosoureas, platinum complexes, no classic alkylators, substituted urea, antitumor antibiotics, microtubule agents, and asparaginase.

55. (Canceled)

56. (Previously presented) A polymeric structure comprising the oxidized heparin fraction of claim 1, wherein said oxidized heparin fraction is covalently attached to the polymeric structure by surface grafting or copolymerization, non-covalently incorporated into a matrix of the polymeric structure, or encapsulated as a biomedical material within the polymeric structure.

57. (Previously presented) The polymeric structure of claim 56, wherein said oxidized heparin fraction is non-covalently incorporated into the matrix.

58. (Previously presented) The polymeric structure of claim 57, wherein the matrix comprises a biocompatible polymer and provides for a sustained release of said oxidized heparin fraction.

59. (Previously presented) The polymeric structure of claim 58, wherein said biocompatible polymer is ethylene vinyl acetate.

60. (Canceled)

61. (Previously presented) The polymeric structure of claim 56, wherein said oxidized heparin fraction is covalently attached to the polymeric structure by surface grafting.

62. (Previously presented) The polymeric structure of claim 56, wherein said oxidized heparin fraction is covalently attached to the polymeric structure by copolymerization.

63. (Previously presented) The polymeric structure of claim 56, wherein said oxidized heparin fraction is encapsulated as said biomedical material within the polymeric structure.

64. (Withdrawn) A method for treating a subject, comprising administering the polymeric structure of claim 56 to the subject to: inhibit angiogenesis in the subject, treat an angiogenesis-mediated disorder in the subject, or both inhibit angiogenesis in the subject and treat said angiogenesis-mediated disorder in the subject.

65. (Withdrawn) The method of claim 64, wherein the subject is a human.
66. (Withdrawn) The method of claim 64, wherein the subject is a mammal.
67. (Withdrawn) The method of claim 64, wherein the subject is a non-mammalian animal.
68. (Withdrawn) The method of claim 64, wherein said administering comprises administering the polymeric structure to the subject orally, parenterally, transdermally, subcutaneously, intravenously, intramuscularly, intraperitoneally, by intravascular instillation, intraocularly, intranasally, intraarterially, intralésionally, or by application of the polymeric structure to mucous membranes of the subject.
69. (Withdrawn) The method of claim 64, wherein said administering comprises administering the polymeric structure to the subject with a pharmaceutically acceptable carrier, excipient, or stabilizer.
70. (Withdrawn) The method of claim 64, wherein administering comprises administering the polymeric structure to the subject to inhibit angiogenesis in the subject
71. (Withdrawn) The method of claim 64, wherein administering comprises administering the polymeric structure to the subject to treat said angiogenesis-mediated disorder in the subject.

72. (Withdrawn) The method of claim 64, wherein the angiogenesis-mediated disorder is selected from the group consisting of tumors, cancer, ocular neovascular-disorders, inflammatory disorders, endometriosis, retrolental fibroplasia, rubeosis, capillary proliferation in atherosclerotic plaques or osteoporosis, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophilic joints, and wound granulation.

73. (Withdrawn) A method for treating a subject, comprising administering the oxidized heparin fraction of claim 1 to the subject to: inhibit angiogenesis in the subject, treat an angiogenesis-mediated disorder in the subject, or both inhibit angiogenesis in the subject and treat said angiogenesis-mediated disorder in the subject.

74. (Withdrawn) The method of claim 73, wherein the subject is a human.

75. (Withdrawn) The method of claim 73, wherein the subject is a mammal.

76. (Withdrawn) The method of claim 73, wherein the subject is a non-mammalian animal.

77. (Withdrawn) The method of claim 73, wherein said administering comprises administering the oxidized heparin fraction to the subject orally, parenterally, transdermally, subcutaneously, intravenously, intramuscularly, intraperitoneally, by intravascular instillation, intraocularly, intranasally, intraarterially, intralesionally, or by application of the oxidized heparin fraction to mucous membranes of the subject.

78. (Withdrawn) The method of claim 73, wherein said administering comprises administering the oxidized heparin fraction to the subject with a pharmaceutically acceptable carrier, excipient, or stabilizer.

79. (Withdrawn) The method of claim 73, wherein administering comprises administering the oxidized heparin fraction to the subject to inhibit angiogenesis in the subject

80. (Withdrawn) The method of claim 73, wherein administering comprises administering the oxidized heparin fraction to the subject to treat said angiogenesis-mediated disorder in the subject.

81. (Withdrawn) The method of claim 73, wherein the angiogenesis-mediated disorder is selected from the group consisting of tumors, cancer, ocular neovascular-disorders, inflammatory disorders, endometriosis, retrolental fibroplasia, rubeosis, capillary proliferation in atherosclerotic plaques or osteoporosis, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophiliac joints, and wound granulation.

82. (Withdrawn) A method for treating a subject, comprising administering the composition of claim 43 to the subject to: inhibit angiogenesis in the subject, treat an angiogenesis-mediated disorder in the subject, or both inhibit angiogenesis in the subject and treat said angiogenesis-mediated disorder in the subject.

83. (Withdrawn) The method of claim 82, wherein the subject is a human.

84. (Withdrawn) The method of claim 82, wherein the subject is a mammal.

85. (Withdrawn) The method of claim 82, wherein the subject is a non-mammalian animal.

86. (Withdrawn) The method of claim 82, wherein said administering comprises administering the composition to the subject orally, parenterally, transdermally, subcutaneously, intravenously, intramuscularly, intraperitoneally, by intravascular instillation, intraocularly, intranasally, intraarterially, intralesionally, or by application of the composition to mucous membranes of the subject.

87. (Withdrawn) The method of claim 82, wherein said administering comprises administering the composition to the subject with a pharmaceutically acceptable carrier, excipient, or stabilizer.

88. (Withdrawn) The method of claim 82, wherein administering comprises administering the composition to the subject to inhibit angiogenesis in the subject.

89. (Withdrawn) The method of claim 82, wherein administering comprises administering the composition to the subject to treat said angiogenesis-mediated disorder in the subject.

90. (Withdrawn) The method of claim 82, wherein the angiogenesis-mediated disorder is selected from the group consisting of tumors, cancer, ocular neovascular-disorders, inflammatory disorders, endometriosis, retrolental fibroplasia, rubeosis, capillary proliferation in

atherosclerotic plaques or osteoporosis, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophilic joints, and wound granulation.

91. (New) The oxidized heparin fraction of claim 1, wherein the sulfate to carboxylate ratio is about 5:1.

92. (New) The oxidized heparin fraction of claim 1, wherein from about 50% to about 100% of primary hydroxyls in glucosamine residues and secondary hydroxyl groups in disaccharide units are substituted by O-sulfate esters in the O-sulfated oxidized heparin fraction.

93. (New) The oxidized heparin fraction of claim 1,

wherein the anticoagulant reduction characteristic comprises a first anticoagulant reduction characteristic, a second anticoagulant reduction characteristic, or a combination thereof;

wherein the first anticoagulant reduction characteristic is that the oxidized heparin fraction reduces a mean percent inhibition of platelet clot strength by factor of at least about 8 relative to a mean percent inhibition of platelet clot strength of unfractionated heparin under a condition of the concentration of the oxidized heparin fraction in human blood being equal to the concentration of the unfractionated heparin in human blood;

wherein the second anticoagulant reduction characteristic is that the oxidized heparin fraction reduces a prolongation of clotting time of human blood by at least 75% relative to a prolongation of clotting time of human blood by unfractionated heparin under a condition of the concentration of the oxidized heparin fraction in human blood being equal to the concentration of

the unfractionated heparin in human blood, subject to the clotting time being a prothrombin time (PT) or an activated partial thromboplastin time (APTT); and

wherein the angiogenesis inhibition characteristic is that the oxidized heparin fraction in an endothelial cell (EC) growth medium cancels an effect of recombinant human fibroblast growth factor (FGF2) on EC tube formation in the EC growth medium under a condition of the concentration of FGF2 in the EC growth medium being sufficient to increase a length or area of the EC tube formation by a factor of at least about 2 if the oxidized heparin fraction is not in the EC growth medium.

94. (New) A method, comprising forming the oxidized heparin fraction of claim 1, wherein said forming the oxidized heparin fraction comprises O-sulfating the first oxidized heparin fraction by performing sulfate substitution at oxygen bonds at vertexes of repeating units of the first oxidized heparin fraction.